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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
08/823,999	03/25/97	ROGERS C	MIT7501

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EXAMINER	
GAMBEL, P.	
ART UNIT	**PAPER NUMBER**
1644	14

DATE MAILED: 08/16/99

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☑ Responsive to communication(s) filed on 5/28/99

☑ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☑ Claim(s) 1-12 is/are pending in the application.
Of the above, claim(s) 7,9 is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☑ Claim(s) 1-6, 8, 10-12 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☑ Notice of Reference Cited, PTO-892
☑ Information Disclosure Statement(s), PTO-1449, Paper No(s). 11
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

DETAILED ACTION

1. Applicant's amendment, filed 5/28/99 (Paper No. 13), is acknowledged.
Claims 13-17 have been canceled.

Claims 1-6, 8, 10-12 and the species of antibodies to MAC-1 are under consideration as being drawn to the elected invention.

Claims 7 and 9 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a nonelected invention

Applicant's submission, filed 5/28/99 (Paper No. 13), is in compliance with the Sequence Rules.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.
This Office Action will be in response to applicant's arguments, filed 5/28/99 (Paper No. 13).
The rejections of record can be found in the previous Office Action (Paper No. 10).

3. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed, including the specificity of claimed/elected compounds.
Applicant's amendment, filed 5/28/99 (Paper No. 13), deferring this issue is acknowledged

4. Formal drawings, filed 6/1/98, are acceptable.

5. Claims 1-6, 8, 11 and 12 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention as the claims read on "a compound which specifically inhibits or reduces leukocyte-integrin-mediated adhesion for the reasons of record set forth in Paper No. 10).

Applicant's arguments, filed 5/28/99 (Paper No. 13), have been fully considered but are not found convincing. Applicant argues that the literature supports animal models as predictive of efficacy and that there are numerous protein therapies.

Applicant is reminded that the rejection is not drawn to the elected invention of anti-Mac1 antibodies but rather drawn to "a compound which specifically inhibits or reduces leukocyte-integrin-mediated adhesion".

In view of the lack of predictability of the art to which the invention pertains the lack of established clinical protocols for effective adhesion-based therapies, undue experimentation would be required to practice the claimed methods with a reasonable expectation of success, absent a specific and detailed description in applicant's specification of how to effectively practice the claimed methods and absent working examples providing evidence which is reasonably predictive for the breadth of compounds which specifically inhibits or reduces leukocyte-integrin-mediated adhesion.

Applicant's arguments are not found persuasive with respect to the breadth of "compounds which specifically inhibits or reduces leukocyte-integrin-mediated adhesion".

6. Claims 1-6, 8 and 10-12 stand rejected under 35 U.S.C. § 102(e) as being anticipated by Coller et al. (U.S. Patent No. 5,770,198), as further evidenced by Simon et al. (Circulation, 1995).for the reasons of record set forth in Paper No. 10). Coller et al. teaches the use of the 7E3 antibody to treat a number of thrombotic conditions (see entire document, including Utility of Platelet-Specific Chimeric immunoglobulin in columns 5-7). Simon et al. provides evidence that the 7E3 antibody cross-reacts with Mac-1 (see entire document).

Applicant's arguments, filed 5/28/99 (Paper No. 13), have been fully considered but are not found convincing. Applicant argues in conjunction with Deitch et al. (Arterioscler. Thromb. Vasc. Biol. 18: 11730 -1737, 1998; Abstract only) that the results obtained with c7E3 were not from inhibition of intimal hyperplasia or improved artery wall remodeling".

In contrast to applicant's assertions, Simon et al. (Arterioscler. Thromb. Vasc. Biol. 17: 528-535, 1997) and Genetta et al. (Annals of Pharmacology 30: 251 -257, 1996) both acknowledged that 7E3 reduced clinical restenosis (see Abstracts). Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations of inhibiting or reducing stenosis or restenosis would be inherent properties of the referenced methods using 7E3 antibodies.

Applicant's arguments are not found persuasive.

7. Claims 1-6, 8 and 10 stand rejected under 35 U.S.C. § 102(e) as being anticipated by Simon et al. (Circulation, 1995) for the reasons of record set forth in Paper No. 10). Simon et al. teaches that the 7E3 antibody is used to inhibit ischemic complications of coronary angioplasty and clinical restenosis and that this 7E3 antibody cross-reacts with Mac-1 (see Abstract).

Applicant's arguments, filed 5/28/99 (Paper No. 13), have been fully considered but are not found convincing. Applicant argues in conjunction with Deitch et al. (Arterioscler. Thromb. Vasc. Biol. 18: 11730 -1737, 1998; Abstract only) that the results obtained with c7E3 were not from inhibition of intimal hyperplasia or improved artery wall remodeling".

In contrast to applicant's assertions, Simon et al. (Arterioscler. Thromb. Vasc. Biol. 17: 528-535, 1997) and Genetta et al. Annals of Pharmacology 30: 251 -257 (1996) both acknowledged that 7E3 reduced clinical restenosis (see Abstracts). Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations of inhibiting or reducing stenosis or restenosis would be inherent properties of the referenced methods using 7E3 antibodies.

Applicant's arguments are not found persuasive.

8. Claims 1-6, 8, 10-12 stand rejected under 35 U.S.C. § 103 as being unpatentable over Ricevuti et al. (Artherosclerosis, 1991) AND/OR Albelda et al. (FASEB J., 1994) AND/OR Coller et al. (U.S. Patent No. 5,770,198) AND/OR Simon et al. (Circulation, 1995) in view of art known use of administering pharmaceutical reagents in various composition forms and at various intervention times and in further evidence of Neumann et al. (JACC, 1996) for the reasons of record set forth in Paper No. 10).

Applicant's arguments, filed 5/28/99 (Paper No. 13), have been fully considered but are not found convincing. Applicant argues in conjunction with Deitch et al. (Arterioscler. Thromb. Vasc. Biol. 18: 11730 -1737, 1998; Abstract only) that the results obtained with c7E3 were not from inhibition of intimal hyperplasia or improved artery wall remodeling".

In contrast to applicant's assertions, Simon et al. (Arterioscler. Thromb. Vasc. Biol. 17: 528-535, 1997) and Genetta et al. Annals of Pharmacology 30: 251 -257 (1996) both acknowledged that 7E3 reduced clinical restenosis (see Abstracts). The claimed functional limitations of inhibiting or reducing stenosis or restenosis would be properties of the referenced methods using 7E3 antibodies.

Applicant argues that Ricevuti al. Relates to ischemia and reperfusion, not restenosis

Applicant argues Albelda does not mention restenosis

Applicant argues that Neumann et al. Indicates generally that were was neutrophil and platelet activation at the injured artery.

Applicant argues that results obtained relative to ischemia and reperfusion are not predictive of results obtained in the treatment of restenosis; that is, the mechanism are different, the treatments are different and the outcomes are different.

In contrast to applicant's assertions, the combination of the prior art did provide the ordinary artisan with motivation and an expectation of success that the use of anti-Mac-1 specific antibodies would inhibit stenosis and restenosis associated with vascular intervention given that a property of the 7E3 antibody was to bind and inhibit via the Mac-1 specificity (Coller et al. and Simon et al.); that the Mac-1 specificity was an important target in treating complications associated with vascular intervention (Neumann et al.) ; that inhibiting PMNs via anti-CD11b/CD18 antibodies inhibited ischemia-reperfusion injury (Ricevuti et al.); that the use of adhesion molecule-specific including blockade of the CD11/CD18 complex had been show to inhibit neutrophil influx in almost every system to date including the heart and ischemia reperfusion (see Albelda).

The arguments of applicant's representative cannot take the place of evidence in the record Applicant's reliance on unexpected results do not overcome clear and convincing evidence of obviousness

Applicant's arguments are not found persuasive for the reasons of record.

9. No claim is allowed.

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

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August 10, 1999

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